

In the claims

The following amendments are made with respect to the claims in the International application PCT/EP2004/011503.

This listing of claims will replace all prior versions and listings of claims in this application.

1 (currently amended). ~~[[In]]~~ An *in vitro* method for analyzing a sample from a mammal in connection with at least one cardiovascular diseases disease, wherein said method comprises the following steps:

a) isolating ~~[[of]]~~ bone marrow-precursor-cells (BMP) and/or blood-derived circulating precursor-cells (BDP) by means of at least one cell specific surface markers marker, and

b) determining ~~[[of]]~~ the cardiovascular functionality of the isolated BMP and/or BDP by means of a suitable migration assay.

2 (currently amended). ~~Method~~ The method according to claim 1, further comprising the comparison of the result as obtained from the sample as examined with a reference value and/or the result of a reference sample.

3 (currently amended). ~~Method~~ The method according to claim 1-~~or~~ 2, wherein the sample to be examined is derived from a human.

4 (currently amended). ~~Method~~ The method according to ~~any of claims 1 to 3~~ claim 1, wherein the sample to be examined is selected from the group consisting of bone marrow, peripheral blood or fractions thereof and cell culture-suspensions or fractions thereof.

5 (currently amended). ~~Method~~ The method according to claim 4, wherein a coagulation inhibitor, ~~in particular Heparin or EDTA,~~ is added to the peripheral blood.

6 (currently amended). ~~Method~~ The method according to claim 4, wherein the sample to be examined is obtained by means of punctuation from the bone marrow.

7 (currently amended). ~~Method according to any of claims 1 to 6~~ The method according to claim 1, wherein the isolating occurs by using density-gradient-centrifugation, cell specific surface markers, and/or immunological methods.

8 (currently amended). ~~Method~~ The method according to claim 7, wherein the isolating occurs by using FACS or immunomagnetic separation.

9 (currently amended). ~~Method according to any of claims 1 to 8~~ The method according to claim 1, wherein the cell specific surface marker for BMP is selected from CD34, CD45 ~~and/or~~ and CD133, and for BDP is selected from VEGFR2, CD105, vWF ~~and/or~~ and CD31.

10 (currently amended). ~~Method according to any of claims 1 to 9~~ The method according to claim 1, wherein the migration assay is performed in a Boyden-chamber or a modified Boyden-chamber.

11 (currently amended). ~~Method according to any of claims 1 to 10~~ The method according to claim 1, wherein the migration assay is performed [[by]] using SDF-1, VEGF, ~~SDF-1 or~~ PIGF or MCP-1.

12 (currently amended). ~~Method according to any of claims 1 to 11~~ The method according to claim 1, wherein the cardiovascular ~~diseases are~~ disease is selected from the group consisting of stable and unstable angina, stable coronary heart disease, acute coronary syndrome, myocardial infarction, acute myocardial infarction, acute heart syndrome, coronary artery disease, chronic ischemic cardiomyopathy (ICMP), dilatative cardiomyopathy (DCM), heart insufficiency, [[or]] and other causes of a cardiac weakness.

13 (currently amended). ~~Method according to any of claims 1 to 12~~ The method according to claim 1, wherein the method is performed immediately before a cell infusion into the mammal.

14 (currently amended). ~~Method according to any of claims 1 to 13~~ The method according to claim 1, wherein the examined isolated BMP and/or BDP are autologous and/or heterologous for the mammal.

15 (currently amended). ~~Diagnostic~~ A diagnostic kit, comprising means for performing ~~the method according to any of claims 1 to 14~~ an *in vitro* method for analyzing a sample from a mammal in connection with at least one cardiovascular disease, wherein said method comprises the following steps:

- a) isolating bone marrow-precursor-cells (BMP) and/or blood-derived circulating precursor-cells (BDP) by means of at least one cell specific surface marker, and
- b) determining the cardiovascular functionality of the isolated BMP and/or BDP by means of a migration assay,

optionally together with additional components and/or excipients.

16 (currently amended). ~~Use of the kit according to claim 15~~ A method for diagnosing and/or prognosing cardiovascular diseases, for monitoring ~~of their~~ therapies and/or for the determination of the cardiovascular functionality of BMPs or BDPs for a stratification for a prospective cell therapy with stem- and progenitor cells for increasing the perfusion of ischemic tissue or for the regeneration of tissue loss in particular in heart insufficiency, and/or for identifying ~~[[of]]~~ patients that would profit ~~[[fro]]~~ from an *ex vivo* pretreatment of their BMPs or BDPs for an improvement of the cardiovascular functionality before retransplantation of the cells.

17 (currently amended). ~~[[In]]~~ An *in vitro* method for isolating ~~specific~~ bone marrow-precursor-cells (BMPs) and/or blood-derived circulating precursor-cells (BDPs), comprising:

- a) taking ~~[[of]]~~ a sample from a donor-mammal,
- b) isolating BMPs and/or BDPs from the sample so obtained, and
- c) determining ~~[[of]]~~ the cardiovascular functionality of the isolated BMPs and/or BDPs by means of a ~~suitable~~ migration assay.

18 (currently amended). ~~Method~~ The method according to claim 17, wherein the sample to be examined is derived from a human.

19 (currently amended). ~~Method~~ The method according to claim 17 ~~or 18~~, wherein the sample to be examined is selected from the group consisting of bone marrow, peripheral blood or fractions thereof and cell culture-suspensions or fractions thereof.

20 (currently amended). ~~Method~~ The method according to claim 19, wherein the sample to be examined is obtained by means of punctation from the bone marrow.

21 (currently amended). ~~Method according to any of claims 17 to 20~~ The method according to claim 17, wherein the isolating occurs by means of density-gradient-centrifugation, cell specific surface markers, and/or immunological methods.

22 (currently amended). ~~Method~~ The method according to claim 21, wherein the isolating occurs by using FACS or immunomagnetic separation.

23 (currently amended). ~~Method according to any of claims 17 to 22~~ The method according to claim 17, wherein ~~[[the]]~~ said isolating step utilizes a cell specific surface marker for BMP ~~[[is]]~~ selected from CD34, CD45 ~~and/or~~ and CD133, and for BDP ~~[[is]]~~ selected from VEGFR2, CD105, vWF ~~and/or~~ and CD31.

24 (currently amended). ~~Method according to any of claims 17 to 23~~ The method according to claim 17, wherein the migration assay is performed in a Boyden-chamber or a modified Boyden-chamber.

25 (currently amended). ~~Method according to any of claims 17 to 24~~ The method according to claim 17, wherein the migration assay is performed by using SDF-1, VEGF, ~~SDF-1 or~~ PlGF or MCP-1.

26 (currently amended). ~~Method according to any of claims 17 to 25~~ The method according to claim 17, wherein the isolated BMP and/or BDP are ~~further~~ genetically modified, ~~in particular~~ in order to improve the cardiovascular functionality of the cells.

27 (currently amended). ~~Specific~~ A bone marrow-precursor-cell (BMP) or blood-derived circulating precursor-cell (BDP), ~~produced~~ obtained according to any of claims 17 to 26 ~~an~~ in vitro method for isolating specific bone marrow-precursor-cells (BMPs) and/or blood-derived circulating precursor-cells (BDPs), comprising:

- a) taking a sample from a donor-mammal,
- b) isolating BMPs and/or BDPs from the sample so obtained, and

c) determining the cardiovascular functionality of the isolated BMPs and/or BDPs by means of a migration assay.

28 (currently amended). ~~Specify~~ The bone marrow-precursor-cell (BMP) or blood-derived circulating precursor-cell (BDP) according to claim 27, wherein the isolated BMPs and/or isolated BDPs are autologous and/or heterologous for the mammal.

29 (currently amended). ~~Method~~ A method for producing a pharmaceutical composition, comprising the method according to any of claims 1 to 26 obtaining a sample from a mammal, wherein said obtaining comprises the following steps:

- a) isolating bone marrow-precursor-cells (BMP) and/or blood-derived circulating precursor-cells (BDP) by means of at least one cell specific surface marker, and
- b) determining the cardiovascular functionality of the isolated BMP and/or BDP by means of a migration assay

and furthermore formulating ~~[[of]]~~ said pharmaceutical composition by admixing with ~~common~~ pharmaceutically acceptable carries and/or diluents.

30 (currently amended). ~~Method~~ The method according to claim 29, wherein formulating furthermore comprises an admixing with ~~statines, in particular atorvastatin~~ a statin, VEGF and/or erythropoietin.

31 (currently amended). ~~Pharmaceutical~~ A pharmaceutical composition, produced according to claim 29 or 30 by obtaining a sample from a mammal, wherein said obtaining comprises the following steps:

- a) isolating bone marrow-precursor-cells (BMP) and/or blood-derived circulating precursor-cells (BDP) by means of at least one cell specific surface marker, and
- b) determining the cardiovascular functionality of the isolated BMP and/or BDP by means of a migration assay

and furthermore formulating said pharmaceutical composition by admixing with pharmaceutically acceptable carries and/or diluents.

32 (currently amended). ~~Use of a specific BMP and/or BDP according to claim 27 or 28 or a pharmaceutical composition according to claim 31~~ A method for the treatment of a

cardiovascular diseases disease, selected from the group consisting of stable and unstable angina, stable coronary heart disease, acute coronary syndrome, myocardial infarction, acute myocardial infarction, acute heart syndrome, coronary artery disease, chronic ischemic cardiomyopathy (ICMP), dilatative cardiomyopathy (DCM), heart insufficiency, [[or]] and other causes of a cardiac weakness, wherein said method comprises administering to a mammal in need of such treatment,

a bone marrow-precursor-cell (BMP) or blood-derived circulating precursor-cell (BDP), obtained by an *in vitro* method comprising:

- a) taking a sample from a donor-mammal,
- b) isolating BMPs and/or BDPs from the sample so obtained, and
- c) determining the cardiovascular functionality of the isolated BMPs and/or BDPs by means of a migration assay.

33 (currently amended). [[Use]] The method according to claim 32, wherein the treatment comprises the infusion of cells into the mammal.

34 (currently amended). [[Use] The method according to claim 32, wherein the treatment furthermore comprises the administration of statines, in particular atorvastatin, VEGF, and/or erythropoietin.